Psychiatric comorbidity: is more less?

HAROLD ALAN PINCUS[1,3], JAMES D. TEW, JR.[1], MICHAEL B. FIRST[2]

[1]Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
[2]Department of Psychiatry, Columbia University, New York, NY, USA
[3]RAND - University of Pittsburgh Health Initiative, Pittsburgh, PA, USA

With each successive revision of the DSM and ICD, psychiatric comorbidity has become more prevalent. The 'atheoretical' approaches of the DSM and ICD explicitly encourage multiple diagnoses with few exclusionary hierarchies, in the hope that all clinically relevant information will be captured. However, the current strategy of diagnosing 'maximal' comorbidity may not reflect 'optimal' comorbidity. Many clinicians and health information systems, particularly those in developing countries, have a limited capacity for capturing this diagnostic information, and fail to characterize additional diagnoses that are present. This article will address the evolution of our current diagnostic system as a way of understanding the emergence of comorbid psychiatric diagnoses. Alternative diagnostic approaches (a dimensional system, diagnostic hierarchies, and mixed diagnostic categories) that could be used to address the emergence of comorbid psychiatric diagnoses are considered. Future challenges for the next evolution of DSM and ICD are presented.

Key words: Psychiatric diagnosis, comorbidity

Since the revision of the DSM-III, there has been an apparent significant increase in the prevalence of comorbid psychiatric diagnoses. In the literature, much attention has been given to the co-occurrence of mood and anxiety disorders, psychosis and substance use disorders, as well as among the Axis II diagnoses, to name a few.

This article will examine the evolution of our current diagnostic system as a way of understanding the emergence of comorbid psychiatric diagnoses. Using clinical examples, we will explore several alternate strategies for reducing psychiatric comorbidity that could be implemented in place of the current one, and consider strengths and weaknesses of each.

The concept of comorbidity certainly is not unique to psychiatry. Feinstein (1) coined the term comorbidity as 'any distinct additional clinical entity that has existed or that may occur during the clinical course of a patient who has the index disease under study'. A simple example would be a patient with chronic obstructive pulmonary disease and diabetes mellitus.

In psychiatry, when distinct symptoms like anxiety and depression co-occur, whether they indicate the presence of two distinct clinical entities or whether they are two components of a single disorder is mostly a matter of speculation, as we know little about the etiology and pathophysiologic interrelationship of mental illnesses. For example, does the patient who binges and purges and also abused alcohol really have two distinct mental illnesses (what we might view as 'true comorbidity', as defined by Feinstein), or are they both the manifestations of a primary disorder of impulse control?

In recognition of this lack of knowledge, the diagnostic systems that are in current use (DSM-IV and ICD-10) are broad, descriptive, and have relatively few exclusionary hierarchies (whereby one disorder is assumed to be responsible for, and therefore supercedes the diagnosis of, another).

The DSM-IV employs the basic strategy that, given the absence of knowledge about the underlying nature of psychiatric disorders, clinicians should convey the maximum amount of descriptive information possible. According to the DSM-IV, a patient who drinks heavily, has severe and recurrent depressive episodes, binges and purges, and has panic attacks, would be assigned four separate Axis I diagnoses (as opposed to a single, all-encompassing diagnosis like "severe neurotic disorder" that might incorporate all of these symptoms). In the above case, giving four diagnoses might emphasize that each of these problems needs to be addressed in the treatment plan. This fact might be obscured if a single less descriptive diagnosis was imposed.

At its best, our current diagnostic system has the potential to communicate large amounts of detailed clinical information about patients with complex problems, allowing for targeted treatments and more precisely defined study populations. At its worst, it can be overwhelming to clinicians and health information systems, and obscure the focus of our treatments by 'losing the forest for the trees'.

HISTORICAL CONTEXT

With each successive revision from DSM-I to DSM-IV, psychiatric comorbidity has become more prevalent. The reason lies in the design of the diagnostic system itself: the DSM-IV is a descriptive, categorical system that splits psychiatric behaviors and symptoms into numerous distinct diagnoses, and employs few exclusionary hierarchies to eliminate multiple diagnoses.

The original version of the DSM was a descriptive system that incorporated many of the concepts and the structure of Emil Kraepelin's classifications of mental disorders. Compared to subsequent revisions, the DSM-I and DSM-II followed a "one disease-one diagnosis" model in which the clinician strived to assign a single all-encompassing diagnosis, using qualifying phrases (such as: "with neurotic reaction" and "with psychotic reaction") to describe complex cases.

Qualifying phrases from other categories could be applied to any of the major diagnoses to 'lump' symptoms into fewer, broader categories. For example, 'schizophrenic reaction, hebephrenic type, with neurotic reaction' might be used to describe a patient with a primary diagnosis of schizophrenia who also shows clinically significant depressive symptoms. In another example from DSM-I, a patient with different types of anxiety symptoms is given a single diagnosis of 'phobic reaction, manifested by claustrophobia, with obsessive-compulsive symptoms, counting and recurring thoughts'.

The DSM-III, however, took a different approach of cutting the diagnostic pie into small slices, adding a large number of relatively narrowly defined psychiatric diagnoses, and supplied operationalized diagnostic criteria for each. For example, the DSM-III split the single DSM-II category 'phobic neurosis' into five DSM-III categories: agoraphobia with panic, agoraphobia without panic, social phobia, simple phobia, and separation anxiety disorder. Not surprisingly, the number of distinct psychiatric diagnoses described in the DSM-IV is nearly double that of the DSM-II.

Because of the potential for spurious comorbidity that might result from the increase in the overall number of categories, exclusionary criteria were sometimes added to reduce comorbidity in those cases where it was believed that a symptom presentation that met criteria for one disorder was really 'due to' another disorder. For example, the criteria for agoraphobia indicate that the diagnosis should not be given if the characteristic avoidant behavior is really due to obsessive-compulsive disorder and a diagnosis of panic disorder is not given if the panic attacks are really due to major depression. However, the use of the phrase 'due to' in these exclusion criteria forced the clinician to determine when a symptom was attributable to one disorder versus another, a decision based on assumptions about causality that are not empirically-based. Resulting partly from research conducted by Boyd (2) in the 1970s and 1980s, many of the underlying assumptions about the relationship between mood and anxiety symptoms came into question. In subsequent revisions of the DSM, starting with the DSM-III-R, an increasing recognition that the existing diagnostic hierarchies were not based on empirical data led to the removal of many (though not all) exclusion criteria.

The ultimate result of this combination of widespread diagnostic splitting and the spare use of diagnostic hierarchies is the common occurrence that patients qualify for multiple diagnoses. In a study involving 500 subjects presenting for intake in a general psychiatric clinic, Zimmerman and Mattia (3), using semi-structured clinical interviews, noted that more than a third of the patients qualified for three or more Axis I disorders.

Psychiatric comorbidity is, in fact, explicitly encouraged in the DSM-IV. According to the 'Use of the Manual' section of the DSM-IV, 'the general convention in DSM-IV is to allow multiple diagnoses to be assigned for those presentations that meet criteria for more than one DSM-IV disorder'. The strategy is to encourage the clinician to record the maximum amount of diagnostic information, as a way of characterizing the complexity of clinical presentations.

Unfortunately, many clinicians and health information systems have a limited capacity for actually capturing this diagnostic information, and instead fail to characterize additional diagnoses that are present (4). Furthermore, recording 5 or 6 diagnoses on a patient's chart may obscure the intended focus of treatment. Many health information systems, particularly those in developing countries, only allow for coding a single diagnosis, with the result that any comorbid diagnoses are ignored. Analysis of diagnostic data collected from such systems may lead to erroneous assumptions being made (e.g., about treatment utilization). For example, consider three patients carrying a primary diagnosis of severe, recurrent, major depressive disorder, each of whom has a different comorbid diagnosis (e.g., obsessive-compulsive disorder; alcohol dependence; gender identity disorder). A system that allows for the recording of only major depression would imply that these three patients were diagnostically homogeneous, when in fact their disparate comorbid diagnoses suggest otherwise.

APPRAISAL OF DSM

Since the ICD-10 diagnostic criteria for research were largely modeled on the DSM-III-R system, with a few key exceptions (i.e., the inclusion of several mixed diagnostic categories like hyperkinetic conduct disorder), the ICD-10 follows the DSM convention regarding psychiatric comorbidity.

The DSM-IV/ICD-10 approach to diagnostic comorbidity has several advantages from a clinical utility perspective. It maximizes the communication of diagnostic information and helps insure that all clinically important aspects of the patient's presentation are addressed. For example, when a patient has symptoms that meet criteria for "major depressive disorder, recurrent, moderate", we can consider specific, evidence-based interventions such as selective serotonin reuptake inhibitor (SSRI) therapy, perhaps combined with individual or group psychotherapy. The specifier "moderate" suggests that the impairment is likely not so severe as to warrant inpatient treatment. If the patient also has symptoms that meet criteria for panic disorder, we might also consider use of a short course of a benzodiazepine until the SSRI takes effect. Going further, if the patient's pattern of substance use also meets criteria for alcohol abuse or dependence, this may give us pause in the use of benzodiazepines to treat her anxiety, as well as cause us to question how much of her depression may be related to her drinking. Lastly, if our assessment reveals that this patient's longstanding pattern of relating to

other people is characteristic of borderline personality disorder, this may help the clinician to form a better sense of long-term prognosis, symptom chronicity, or suggest specific psychotherapies (such as dialectical behavioral therapy).

This clinical example demonstrates how each facet of the diagnostic formulation (reflected in its inclusion in the list of comorbid diagnoses) theoretically can provide a more complete appreciation of the complexity of the patient's clinical presentation, which has the potential to result in more appropriate treatment planning and prognosis.

There is evidence, however, to suggest that much of this diagnostic complexity is not being adequately captured in clinical practice. Zimmerman and Mattia (4) have summarized how several US studies demonstrated that clinicians routinely under-detect psychiatric comorbidity as compared to research assessments using structured diagnostic interviews. One such study found that five times as many comorbid diagnoses were made when using semi-structured interviews as opposed to the clinicians' assessments alone (5). The reasons underlying this discrepancy are probably complex and multifactorial. Many have speculated that, with shrinking reimbursement and more rapid patient flow, psychiatrists lack sufficient time to perform complete diagnostic assessments. It is worth noting that, in Basco's study, the added diagnostic information provided by semi-structured interviews led to a change in patient care in approximately one half of the patients at one month follow-up. This suggests that the comorbid diagnoses were clinically relevant enough to justify a change in the treatment plan.

While it makes intuitive sense that more comprehensive diagnostic information would result in improved patient outcomes, we do not have studies that have investigated this issue. It is likely that psychiatrists in clinical practice are simply choosing not to make certain diagnoses because they do not consider them to be a clinically relevant focus of treatment. For example, the Epidemiological Catchment Area Study, which used a structured interview for its diagnostic assessments, indicated that specific phobia is the most common psychiatric disorder occurring in the US general population (6). Although using structured diagnostic interviews would increase the detection of specific phobia in patients as a comorbid diagnosis, this added information is not likely to be clinically relevant since this is typically not the reason patients seek psychiatric care (4).

Unfortunately, due to our field's limited grasp of how mental disorders interrelate and affect each other's emergence, treatment, and prognosis, we have very little evidence to guide clinicians in how to prioritize multiple co-occurring diagnoses, other than to direct clinicians to use their judgment. For example, DSM-IV provides the following statement: "When (as is often the case) an individual's pattern of behavior meets criteria for more than one Personality Disorder, the clinician should list all relevant Personality Disorder diagnoses in order of importance". But where is the data to guide clinicians in determining which diagnoses are relevant, or which ones are most important? Without such guidance, clinicians must prioritize diagnoses on a case-by-case basis subject to their own clinical judgment. In effect, clinicians apply their own (potentially idiosyncratic) hierarchical rules, resulting in a potential loss of diagnostic reliability and validity.

CLINICAL EXAMPLE: PERSONALITY DISORDERS

A prominent example of excessive comorbidity in the DSM-IV resulting in widespread dissatisfaction among clinicians is in the area of personality disorders (7,8). Using personality disorder diagnosis as a focus, we will describe three alternative approaches to dealing with the problem of comorbidity.

There are 10 distinct personality disorders described in the DSM, with no hierarchical system provided to reduce comorbidity. According to this system, when an individual's pattern of behavior meets criteria for more than one personality disorder, all diagnoses should be listed in order of clinical significance. Widiger (8) has pointed out that certain psychiatric inpatients can be found to meet criteria for 3 to 5, and in some cases up to 7 personality disorders. Using pooled data consisting of 1116 inpatients and outpatients at multiple sites, Stuart et al (9) found that, among those subjects that met criteria for at least one personality disorder, the average number of personality disorder diagnoses was 2.7 (with nearly 10% of subjects meeting criteria for 4 or more). In a study using two separate semi-structured interviews on 100 patients in long-term inpatient treatment, fewer than 15% had only a single personality disorder diagnosis (10).

Despite this, clinicians tend to diagnose personality disorders reductively, even when the patient has sufficient criteria to qualify for two or more specific diagnoses. In a study in which psychiatrists were given case histories on 46 patients that met criteria for 4 personality disorders (for example: borderline, narcissistic, histrionic, and antisocial), two-thirds diagnosed only one, a quarter diagnosed two, and no psychiatrist diagnosed all four (11).

Dimensional approach

An alternative approach to the DSM-IV/ICD-10 categorical method for diagnosing personality disorders is to adopt a dimensional model that depicts the patient's psychopathology as points on a series of fundamental dimensions of psychopathology. The five factor model (FFM) of personality is one externally validated dimensional system that has been proposed as an alternative to the DSM-IV categorical system (12,13). Rather than applying distinct criteria to distinguish 'case' from 'non-case' in each of

a series of personality diagnoses, the clinicians using the FFM rate patients on five major dimensions: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. Within each dimension, there are six 'facets" on which a patient can be rated from 'very high' to 'low'. By using the dimensional model, the FFM system is able to characterize patients in complex ways, without applying multiple labels that imply distinct disorders, each with their own presumed etiology, pathophysiology, and clinical course.

For example, a patient with psychopathology suggestive of borderline, antisocial, and narcissistic personality disorders in the DSM-IV system would instead be characterized as high in 'neuroticism' (with corresponding subscales reflecting propensity for anger, irritability, stress-tolerance, etc.), low in 'agreeableness' (antagonistic), and high in 'openness to experience' (exaggerated mood states, preoccupation with fantasy). Unlike the DSM-IV categorical system that would assign three personality disorder diagnoses to this patient, the FFM method avoids such comorbidity by providing instead a profile indicating patient's place on the continuum of the FFM dimensions.

Furthermore, in contrast to the DSM categorical approach which can suffer from poor diagnostic reliability, especially in cases where patient's personality disorder item count straddles the boundary between case and non-case (e.g., 4 or 5 out of 9 for borderline personality disorder), a personality formulation using the FFM is likely to be more reliable. However, the lack of discrete categories does not lend itself to the study of (ostensibly) distinct clinical populations, and also does not provide a straightforward answer to the question 'does this patient have a personality disorder?'. Providing such a categorical answer to this question is important both for treatment planning (which often requires a categorical judgment of whether or not to treat the patient), and for practical concerns such as determining eligibility for disability. Moreover, most health information systems (e.g. for clinical information or insurance) are not equipped to incorporate dimensional approaches.

Diagnostic hierarchies

Another diagnostic strategy that would reduce comorbidity, alluded to earlier in this article, is to impose additional diagnostic hierarchies. For example, consider the situation where a patient's symptoms meet criteria for both disorder A and disorder B. In the DSM-IV, the patient would receive two diagnoses, A and B. However, if disorder B contained an exclusionary criterion that states it cannot be diagnosed if criteria are also met for disorder A, then only disorder A would be diagnosed. Exclusionary hierarchies are based upon the concept that a single pre-eminent disorder takes precedence over one or more subordinate diagnoses. The underlying assumption is that the symptoms of the subordinate diagnosis are associated features of the primary disorder and thus do not warrant an additional psychiatric diagnosis.

For example, a patient who has suffered from six months of auditory hallucinations combined with persecutory delusions in the absence of mood symptoms is assigned a diagnosis of schizophrenia. The six-month period of non-bizarre delusions also fits the pattern of delusional disorder. However, a diagnostic hierarchy that has schizophrenia take precedence over a diagnosis of delusional disorder prevents a comorbid diagnosis of delusional disorder from also being given. While this hierarchy has not been disputed, others have drawn more criticism, particularly with regard to the relationship between mood and anxiety disorders. Given the dissatisfaction with the excessive comorbidity of personality disorder diagnoses in the DSM, some have recommended that some axis II diagnoses, such as borderline personality disorder, take precedence over other subordinate diagnoses, like dependent or histrionic personality disorder (14).

The problem with imposing diagnostic hierarchies is that they imply certain knowledge of symptom attribution that is at odds with the descriptive approach that is the cornerstone of the DSM. Even some of the remaining hierarchies, such as the exclusion of generalized anxiety disorder in the setting of comorbid major depressive disorder, have continued to draw criticism (15). While expanding the number of diagnostic hierarchies in DSM in order to eliminate all (or virtually all) co-occurring diagnoses would certainly reduce comorbidity, such steps would only be valid if we had an understanding of the etiologies of mental illnesses. Furthermore, such a radical reduction in the number of reported diagnoses risks losing clinically relevant distinctions in complex cases.

Mixed diagnostic categories

Another strategy that has been employed to address comorbidity has been the development of 'mixed' diagnostic categories, which lump together categories that have been separated in the DSM. Research has attempted to identify cases in which apparently co-occurring disorders (by our current diagnostic strategy) may actually reflect a single distinct diagnostic entity, with its own pathogenesis, treatment strategy, and prognosis (16,17). For example, Taylor et al (18) presented data on children referred to a clinic for disruptive or antisocial behavior. They identified that a subset that might otherwise have been characterized as having hyperkinetic syndrome and conduct disorder (by ICD-9 criteria) actually had distinct symptom onset, IQ ratings, neurological exam, and medication responsiveness when compared to the remaining clusters of patients. They used these findings to propose a new diagnosis of 'hyperkinetic conduct disorder' which would be added along with the existing conduct disorder and hyperkinetic categories. Another example includes the

suggestion to combine major depressive disorder and generalized anxiety disorder into a single category, called mixed anxiety/depression (19). One drawback of combining single categories into combined categories based on known co-occurring syndromes is that the number of possible combinations and permutations of categories (in a mathematical sense at least) could easily reach into the thousands.

Another way of combining separate categories that reduces diagnostic comorbidity is to lump categories together into higher order constructs. One example of a 'lumping' diagnostic strategy already in use in the DSM-IV is the combining of the 10 specific personality disorders into three personality disorder 'clusters' based on presumed common characteristics. Clinicians commonly incorporate these clusters into diagnostic formulations, such as 'personality disorder not otherwise specified, with cluster B traits', and researchers have used these mixed categories to delineate patient populations in studies of Axis I comorbidity, treatment responsiveness, and prognosis (20).

The co-occurrence of personality disorders within each cluster is generally higher than between-cluster comorbidity. For example, Stuart et al (9), using data collected in multiple sites on 1116 subjects, found that 73% of patients diagnosed with narcissistic personality disorder also met criteria for histrionic personality disorder, and many met criteria for a third and fourth diagnosis. Under the cluster system, comorbidity of personality disorders is reduced because instead of noting one, two, or three specific personality disorders from cluster B, the clinician would simply note 'cluster B personality disorder' regardless of the number of specific disorders actually present. However, currently, there is insufficient research to justify lumping the personality disorders into clusters for all diagnostic purposes. Furthermore, the widespread introduction of mixed categories whenever certain comorbid combinations are common is unwieldy, given the potentially large number of combined categories that might result.

CONCLUSIONS

More research is needed into the etiology and interrelationship of psychiatric syndromes if we are to understand the full clinical significance of psychiatric comorbidity. In a seminal paper, Robins and Guze (21) posited that diagnostic validity could be improved through increasingly precise clinical description, delineation of syndromes, demographic and biological correlates, and treatment response profiles. Central to this concept was the assertion that empirical evidence would become the mainstay of psychiatric diagnosis. More than three decades later, however, our understanding of the etiology and pathogenesis of mental illness is still very limited. The research that will fully illuminate our understandings of mental illness is still several decades down the road.

As a field, we in psychiatry need to address the implications of our lack of understanding about pathophysiology on the use of our current diagnostic system. The 'atheoretical' approach of the DSM and ICD explicitly acknowledges our incomplete understanding and encourages multiple diagnoses with few exclusionary hierarchies in the hope that all clinically relevant information will be captured.

Unfortunately, this feature also makes the current system quite cumbersome to use as it was intended. Clinicians and health information systems intrinsically place certain information at a higher order of importance than other. Many information systems (especially in developing countries) do not have the capacity for incorporating all comorbidities. Individuals use clinical judgment to prioritize diagnoses, and may fail to account for diagnostic complexity where it exists. However, there is not much guidance for how clinicians make such determinations. As a result, the application of these systems in the real world has veered away from consistency toward more idiosyncratic use. More research is needed if we as a field aspire to accuracy and uniformity in diagnosis. The ultimate goal is to increase the clinical utility of the DSM and ICD in providing better case-conceptualization, communication, and accuracy in prognosis (22).

In another strategy to limit comorbidity, the next editions of the DSM and ICD might add a provision that only those diagnoses that are clinically relevant and that are included as target symptoms in the current treatment plan (or which are useful with respect to prognosis, education, and treatment) should be listed. Again, how to make such differentiations in a consistent manner is not immediately clear and requires future investigation.

In summary, the current strategy of diagnosing 'maximal' comorbidity may not result in 'optimal' comorbidity in terms of best clinical practice. The practice of listing multiple diagnoses has the power to both enhance and obfuscate important clinical information. The next evolution of the DSM needs to balance the current 'rule-based' system with diagnostic strategies that depend on clinical judgment. As the DSM-V and ICD-11 are developed, opportunities for reducing comorbidity by 'lumping' diagnoses (e.g., replacing the 8 specific paraphilias with a single paraphilic disorder with subtypes to indicate specificity, e.g., 'paraphilia, pedophilic and sadistic type') or formalizing a convention for omitting diagnoses from the diagnostic list that are not clinically relevant, should be explored. However, as we move forward in addressing these challenges, we will need to provide explicit decision rules based on systematic assessment of the best data available, or risk reverting to the subjective and impressionistic formulations that were the state of the art fifty years ago with the DSM-I.

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References

1. Feinstein AR. The pre-therapeutic classification of co-morbidity in chronic disease. J Chronic Dis 1970;23:455-68.
2. Boyd JH, Burke JD Jr, Gruenberg E et al. Exclusion criteria of DSM-III: a study of co-occurrence of hierarchy-free syndromes. Arch Gen Psychiatry 1984;41: 983-9.
3. Zimmerman M, Mattia JI. Psychiatric diagnosis in clinical practice: is comorbidity being missed? Compr Psychiatry 1999;40:182-91.
4. Zimmerman M, Mattia JI. Principal and additional DSM-IV disorders for which outpatients seek treatment. Psychiatr Serv 2000;51:1299-304.
5. Basco MR, Bostic JQ, Davies D et al. Methods to improve diagnostic accuracy in a community mental health setting. Am J Psychiatry 2000;157:1599-605.
6. Regier DA, Burke JD. Jr. Psychiatric disorders in the community: the Epidemiological Catchment Area Study. In: Hales RE, Frances AJ (eds). American Psychiatric Association annual review, Vol. 6. Washington: American Psychiatric Association, 1987:610-24.
7. Maser JD, Kaelber C, Weise RE. International use and attitudes toward DSM-III and DSM-III-R: growing consensus in psychiatric classification. J Abnorm Psychol 1991;100:271-9.
8. Widiger TA, Frances AJ, Pincus HA et al (eds). DSM-IV sourcebook, Vol. 4. Washington: American Psychiatric Press, 1998.
9. Stuart S, Pfohl B, Battaglia M et al. The cooccurrence of DSM-III-R personality disorders. J Personal Disord 1998;12: 302-15.
10. Oldham JM, Skodol AE, Kellman HD et al. Diagnosis of DSM-III-R personality disorders by two structured interviews: patterns of comorbidity. Am J Psychiatry 1992;149:213-20.
11. Adler DA, Drake RE, Teague GB. Clinicians' practices in personality assessment: does gender influence the use of DSM-III axis II? Compr Psychiatry 1990; 31:125-33.
12. O'Connor BP, Dyce JA. A test of models of personality disorder configuration. J Abnorm Psychol 1998;107:3-16.
13. Widiger TA, Costa PT. Jr, McCrae RR. A proposal for Axis II: diagnosing personality disorders using the five-factor model. In: Costa PT Jr, Widiger TA (eds). Personality disorders and the five-factor model of personality (2nd ed.) Washington: American Psychological Association, 2002:431-56.
14. Gunderson JG. Diagnostic controversies. In Tasman A, Riba MB (eds). Review of psychiatry, Vol. 11. Washington: American Psychiatric Press, 1992:9-24.
15. Zimmerman M, Chelminski I. Generalized anxiety disorder in patients with major depression: is DSM-IV's hierarchy correct? Am J Psychiatry 2003;160:504-21.
16. Caron C, Rutter M. Comorbidity in child psychopathology: concepts, issues and research strategies. J Child Psychol Psychiatry All Discipl 1991;32:1063-80.
17. Rutter M. Comorbidity: concepts, claims and choices. Criminal Behav Ment Health 1997;7:265-85.
18. Taylor EA, Schachar R, Thorley G et al. Conduct disorder and hyperactivity: I. Separation of hyperactivity and antisocial conduct in British child psychiatric patients. Br J Psychiatry 1986;149: 760-7.
19. Tyrer P. The case for cothymia: an open verdict? Br J Psychiatry 2002;180:380-1.
20. Gude T. Vaglum P. One-year follow-up of patients with cluster C personality disorders: a prospective study comparing patients with 'pure' and comorbid conditions with cluster C, and 'pure' C with 'pure' cluster A or B conditions. J Personal Disord 2001;15:216-28.
21. Robins E, Guze SB. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. Am J Psychiatry 1970;126:983-6.
22. First MB, Pincus HA, Levine JB et al. Using clinical utility as a criterion for revising psychiatric diagnoses. Am J Psychiatry (in press).